IRB Review of Adverse Events

PENN's Response to Managing Adverse Event Reports

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IRB Review of Adverse Events Reports

Purpose of IRB Review

- Determine that the risk-benefit ratio continues to be acceptable
- Determine whether the informed consent document requires revisions
- Determine whether subjects currently enrolled need to be re-consented

"All IRBs recognize and acknowledge this responsibility, but few IRBs are equipped to handle the avalanche of AE reports sent by sponsors via the investigator." Ernest Prentice, et.al., *IRB Management and Function*

PENN Statistics

- PENN receives >250 individual safety reports each week (approximately 13,000 reports each year from industry sponsors (through the PENN Principal Investigator)
- For multi-center industry sponsored clinical trials, the sponsor provides insufficient data in the form of individual safety reports that provide no meaningful context for analyzing individual reports
  - Randomization to test or placebo group may be blinded
  - No denominator

PENN's Perspective

The sponsor, data safety & monitoring board, & investigator are best positioned to assess individual safety reports. This position is supported by the regulations.

- 21 CFR 312.32(c)(1)(a): The sponsor shall notify the FDA and participating investigators of any adverse experience associated with the use of a drug that is both serious, and unexpected.
- 21 CFR 56.108(b)(1): Institutional responsibility to ensure prompt reporting of "any unanticipated problems posing risks to subjects or others

Individual IND Safety Reports

Provide IRB with summary data at the time of continuing review

- External, serious, expected
- External, serious, unexpected, unrelated
- External, serious, unexpected & possibly or definitely not related
- Internal AEs deemed not serious

Promptly INFORM IRB

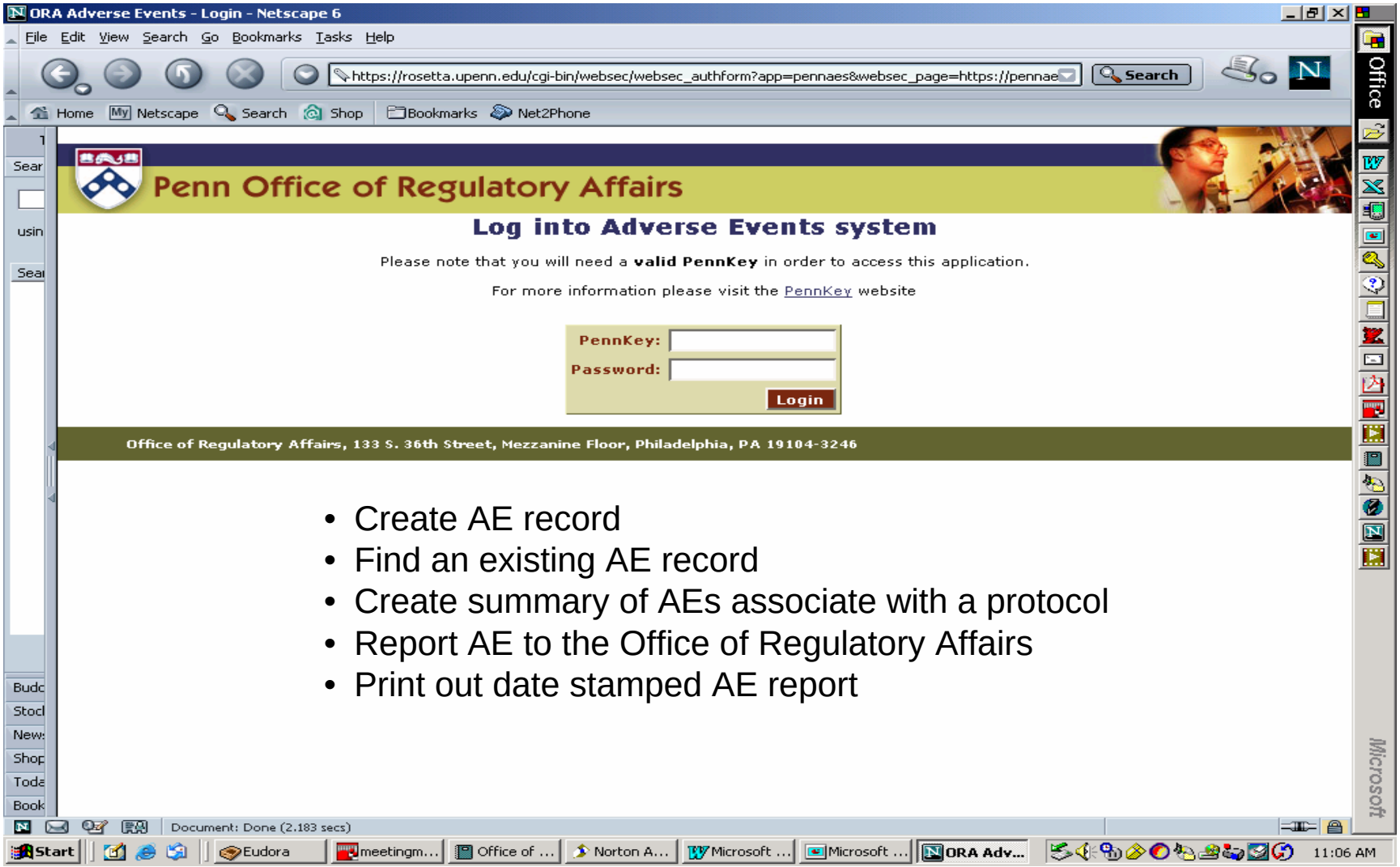
Report to IRB

- Internal serious adverse events regardless of expectedness or relatedness
- External AEs deemed by sponsor or investigator to be serious, unexpected, and probably or definitely related
- Data safety & monitoring reports

PENN AE Reporting System

- Provide a central repository of adverse events information that includes historical and current data.
- Provide the ability to create Notice to Sponsor reports
- Makes the data easily accessible via any web browser
- Provides a tool to monitor and maintain information in a consistent/easily auditable manner
- Facilitate annual reporting
- Provide an immediate date/time stamped electronic report to the Office of Regulatory Affairs

Penn AE System



- Create AE record
- Find an existing AE record
- Create summary of AEs associate with a protocol
- Report AE to the Office of Regulatory Affairs
- Print out date stamped AE report

Penn AE Report

Recommendation to FDA

Consistent with the regulations at 21 CFR, provide clear guidance to industry sponsors on the regulatory requirement to report to the IRB (through the investigator) unanticipated problems that pose risks to subjects or others.

- The sponsor is responsible for assessing adverse events and for providing meaningful, clear, and complete data to assist the IRB in meeting it's regulatory and ethical obligations.
  - *Summary reports*
  - *DSMB reports*